

REMARKS

Sequence Listing

Enclosed herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a Sequence Listing to be inserted into the specification as indicated above. The Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a disk copy of the Sequence Listing. The disk copy of the Sequence Listing, file "1614-0251P.ST25.txt", is identical to the paper copy, except that it lacks formatting.

The amendments made to the specification are intended to reference each amino acid and nucleic acid sequence by a unique SEQ ID NO. The nucleotide sequence on the bottom of page 22 as filed contained two typographical errors. Specifically, nucleotides at positions 37-39 and 106-108 have been amended from "GGA" and "AGG" to "GAA" and "AAG", respectively. These amendments are done to merely correct obvious typographical errors and do not represent new matter.

The Examiner is reminded that corrections to obvious errors are not new matter. Specifically, "an amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction." See MPEP

2163.07(a); In re Oda, 443 F.2d 1200 (CCPA 1971). In the present specification, the nucleotides "GGA" at positions 37-39 on page 22 are said to encode the amino acid "Glu" (glutamic acid). However, it is known in the art that GGA encodes "Gly" (glycine) rather than glutamic acid. Thus, the representation of glutamic acid as being encoded by "GGA" is clearly in error. One of skill in the art would recognize that glutamic acid is actually encoded by the nucleotides "GAA" as indicated by the standard genetic code (copy attached hereto). Similarly, the nucleotides "AGG" at positions 106-108 on page 22 are said to encode the amino acid "Lys" (lysine). However, it is known in the art that AGG encodes "Arg" (arginine) rather than lysine. Thus, the representation of lysine as being encoded by "AGG" is clearly in error. One of skill in the art would recognize that lysine is actually encoded by the nucleotides "AAG" as also indicated by the standard genetic code.

For these reasons, Applicants respectfully submit that the above amendments meet the test as "amendments to correct obvious errors" as set forth in In re Oda. Specifically, one skilled in the art would recognize the nucleotide recitations as errors and would also recognize the appropriate corrections thereto. Entry of the above amendments is therefore respectfully requested.

Restriction Requirement

In response to the Examiner's Restriction Requirement, Applicants elect Group I, claims 1-6 and 21-22, with traverse.

Applicants respectfully submit that the Examiner has not established that there is an undue burden in searching for all claims as required by MPEP § 803. The "undue burden" requirement created by the U.S. Patent and Trademark Office is recited in MPEP § 803:

If the search and examination of an entire application can be made without serious burden, the examiner must examine it on its merits, even though it includes claims to independent and distinct inventions.

Applicants do not believe that an undue burden would be placed on the Examiner to rejoin the claims of Group III to the claims of Group I, specifically because the claims of Groups I and III are both classified in class 424, subclass 275.1. Even if the claims recite hypothetically separate inventions, there is no undue burden for the Examiner to search both within the same application. As such, the Examiner must examine at least the claims of Group I and III on their merits in the present application.

In a similar manner, Group II only consists of two claims (claims 8-9), although classified in a different Class. Nevertheless, it does not appear that restriction practice is necessary, simply for the reason that only two additional claims are sought. Applicants believe that a greater burden exists on the U.S.

Patent and Trademark Office to process (including employee hours and paper requirements) a potential series of three patent applications, directed to the three "inventive groups". It is reasonable to assume that this is not what the U.S. Patent and Trademark Office anticipated when creating restriction practice.

For these reasons, Applicants believe that an undue burden for searching does not exist, and respectfully request that the Examiner rejoin all of the claims of the present invention and examine the claims together in the present application, or at least the claims of Groups I and III. An early and favorable action on the merits of the present application is earnestly solicited.

If the Examiner has any questions concerning this application, the Examiner is requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

Docket No. 1614-0251P

required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17;
particularly, extension of time fees.

Respectfully submitted,

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GMM/KLR/BCF
1614-0251P

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Attachments: Disk Copy of Sequence Listing, Paper Copy of Sequence
Listing, Marked up copy of Changes Made, Standard Genetic Code,
Pages 22 and 23, Copy of the Notice to Comply

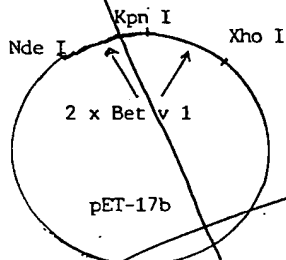
CONSTRUCTION OF THE BET V 1 POLYMERS

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Bet v 1-Dimer

SEQ ID NOS: 13 and 14, respectively:

ATG.....AAC TTG GTA CCG ATG.....AAC TAA
Met Asn Leu Val Pro Met Asn End
Bet v 1 Bet v 1



Bet v 1-Trimer

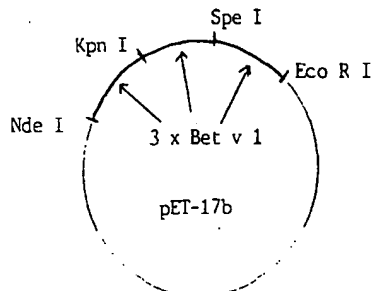
SEQ ID NOS: 15 and 16, respectively:

ATG.....AAC TTG GTA CCG ATG.....AAC CCA CTA GTA ATG.....AAC
Met.....Asn Leu Val Pro Met.....Asn Pro Leu Val Met.....Asn
Bet v 1 Bet v 1 Bet v 1

GAA TTC TGC AGA TAT CCA TCA CAC TGG CGG CCG CTC GAG CAG ATC
Glu Phe Cys Arg Tyr Pro Ser His Trp Arg Pro Leu Glu Gln Ile

CGG CTG CTA ACA AAG CCC GAA AGG AAG CTG AGT TGG CTG CTG CCA
Arg Leu Leu Thr Lys Pro Glu Arg Lys Leu Ser Trp Leu Leu Pro

CCG CTG AGC AAT AAC TAG
Pro Leu Ser Asn Asn End

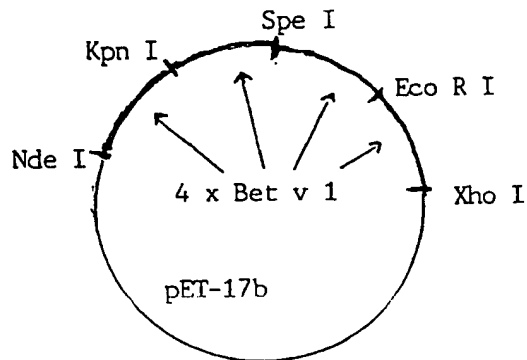


Bet v 1-tetramer

SEQ ID NOS: 17 and 18, respectively:

ATG.....AAC TTG GTA CCG ATG.....AAC CCA CTA GTA ATG.....AAC
Met.....Asn Leu Val Pro Met.....Asn Pro Leu Val Met.....Asn
 Bet v 1 Bet v 1 Bet v 1

GAA TTC ATG.....AAC TAA
 Glu Phe Met.....Asn End
 Bet v 1





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Version With Markings To Show Changes Made

Material being <<added>> is surrounded by << >>, material being ~~deleted~~ is in bolded brackets.

The paragraph on page 6 lines 19-29:

Bet v 1-dimer:

For construction of the first Bet v 1-segment:

5'GAG GAA TTC CAT ATG GGT GTT TTC AAT TAC3' <<(SEQ ID NO:1)>>

Eco R I Nde I

5'CGG GGT ACC AAG TTG TAG GCA TCG GAG TG3' <<(SEQ ID NO:2)>>

Kpn I

For construction of the second Bet v 1-segment:

5'CGG GGT ACC GAT GGG TGT TTT CAA TTA C3' <<(SEQ ID NO:3)>>

Kpn I

5'CCG GAA TTC CCG CTC GAG CTA TTA GTT GTA GGC ATC GGA GTG3'

Eco R I Xho I

<<(SEQ ID NO:4)>>

The paragraph on page 7 lines 5-19:

Second Bet v 1-segment:

[Sequence Id No 1] <<SEQ ID NO:5:>>

5'CGG GGT ACC GAT GGG TGT TTT CAA TTA C3'

Kpn I

[Sequence Id No 2] <<SEQ ID NO:6:>>

5'CGG AAT TCA CTA GTG GGT TGT AGG CAT CGG AGT G3'

Eco R I Spe I

Third Bet v 1-segment:

[Sequence Id No 3] <<SEQ ID NO:7:>>

5'CCG GAA TTC GGA CTA GTA ATG GGT GTT TTC AAT TAC3'

Eco' R I

Spe I

[Sequence Id No 4] <<SEQ ID NO:8:>> 5'CGG AAT TCG TTG TAG GCA TCG GAG TG3'

Eco R I

The paragraph on page 9 lines 4-11:

Results of studies on Bet v 1 polymers

Figure 1. Construction of the Bet v 1 polymers.

The Bet v 1-cDNA (Breiteneder et al., EMBO J. 8 (1989) 1935-1938) was PCR-amplified with [Oligonucleotide] <<oligonucleotide>> primers containing different restriction enzyme cleavage sites. The PCR-products were then ligated as indicated in the figure and subcloned into the plasmid pET-17b (Novagen, Madison, USA). <<Bet v 1-Dimer (SEQ ID NOS: 13 and 14). Bet v 1-Trimer (SEQ ID NOS: 15 and 16) and Bet v 1-Tetramer (SEQ ID NOS: 17 and 18).>>

The paragraph on page 13 lines 19-27:

Figure 8: Two monoclonal anti-Bet v 1-antibodies (moAb A and B) were used together with three synthetic Bet v 1-derived peptides were used in ELISA. The sequences of [th]<<the>> three peptides are shown in the lower part of the figure and corresponds to aa 49-60 <<(SEQ ID NO:19)>>(p17), aa 52-63 <<(SEQ ID NO:20)>>(p18) and aa 55-66 <<(SEQ ID NO:21)>> (p19) of Bet v 1. The peptides were tested for binding to the two Bet v 1 specific monoclonals. The OD values are [displaed] <<displayed>> on the y-axis.

Both moAbs bind to the peptides p18 and p19, which are mapped to the first half of Bet v 1.

The paragraph on page 15 lines 7-16:

Bet v 1 (aa 1-74):

[Sequence Id No 5] <<SEQ ID NO:9:>>

5'GGG AAT TCC ATA TGG GTG TTT TCA ATT AC3'

[Sequence Id No 6] <<SEQ ID NO:10:>>

5'CGG GGT ACC TTA CTC ATC AAC TCT GTC CTT3'

Bet v 1 (aa 75-160):

[Sequence Id No 7] <<SEQ ID NO:11:>>

5'GGG AAT TCC ATA TGG TGG ACC ACA CAA ACT3'

[Sequence Id No 8] <<SEQ ID NO:12:>>

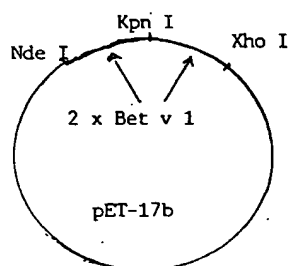
5'CGG GGT ACC TTA GTT GTA GGC ATC GGA3'

CONSTRUCTION OF THE BET V 1 POLYMERS

Bet v 1-Dimer

[Sequence Id Nos 9 and 10,] <<SEQ ID NOS: 13 and 14,>> respectively:

ATG.....AAC	TTG	GTA	CCG	ATG.....AAC	TAA
<u>Met</u>		<u>Asn</u>	Leu Val Pro	<u>Met</u>	<u>Asn</u> End
Bet v 1				Bet v 1	



Bet v 1-Trimer

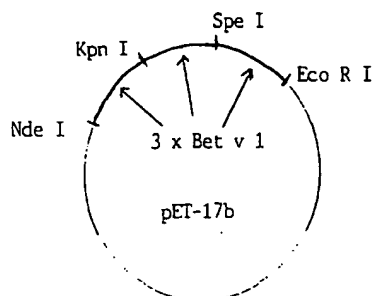
[Sequence Id Nos 11 and 12,] <<SEQ ID NOS: 15 and 16,>> respectively:

ATG.....AAC	TTG	GTA	CCG	ATG.....AAC	CCA	CTA	GTA	ATG.....AAC
<u>Met.....Asn</u>	Leu	Val	Pro	<u>Met.....Asn</u>	Pro	Leu	Val	<u>Met.....Asn</u>
Bet v 1				Bet v 1				Bet v 1

[GGA]<<GAA>> TTC TGC AGA TAT CCA TCA CAC TGG CGG CCG CTC GAG CAG ATC
Glu Phe Cys Arg Tyr Pro Ser His Trp Arg Pro Leu Glu Gln Ile

CGG CTG CTA ACA AAG CCC GAA AGG [AGG]<<AAG>> CTG AGT TGG CTG CTG CCA
Arg Leu Leu Thr Lys Pro Glu Arg Lys Leu Ser Trp Leu Leu Pro

CCG CTG AGC AAT AAC TAG
Pro Leu Ser Asn Asn End

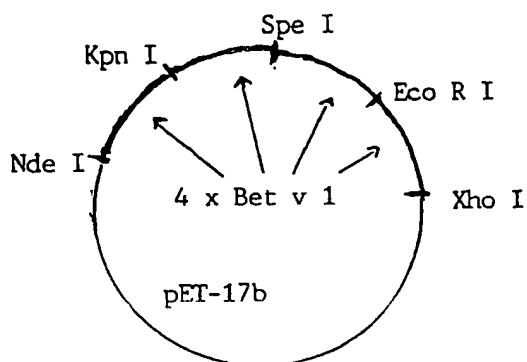


Bet v₁-tetramer

[Sequence Id Nos 13 and 14,] <<SEQ ID NOS: 17 and 18,>> respectively:

ATG.....AAC	TTG	GTA	CCG	ATG.....AAC	CCA	CTA	GTA	ATG.....AAC
<u>Met.....Asn</u>	Leu	Val	Pro	<u>Met.....Asn</u>	Pro	Leu	Val	<u>Met.....Asn</u>
Bet v 1				Bet V 1				Bet v 1

GAA	TTC	ATG.....AAC	TAA
Glu	Phe	<u>Met.....Asn</u>	End
		Bet v 1	



The Standard Genetic Code

FIRST POSITION (5' END)	SECOND POSITION				THIRD POSITION (3' END)
	U	C	A	G	
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met*	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

T → U

*AUG forms part of the initiation signal as well as coding for internal methionine residues.

Names and Abbreviations of the Common Amino Acids

AMINO ACID	THREE-LETTER ABBREVIATION	ONE-LETTER ABBREVIATION
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V